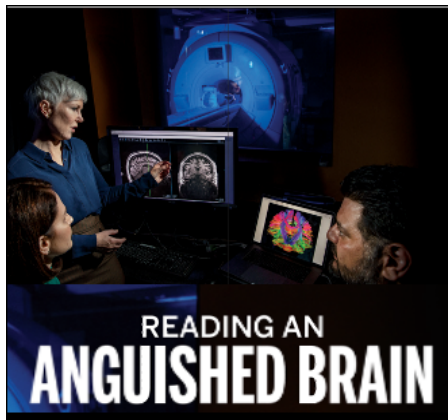


Moonshot for Brain Health

NEUROSCIENCE - INFORMED SOLUTIONS FOR PRECISION MENTAL HEALTH



Restoring hope

Jane, aged 20, had been experiencing depression throughout her teens. The depression worsened when she started college and she had to drop the quarter. Jane had stopped engaging in activities she used to enjoy. She was isolating from friends and family.

Jane was losing all hope and was experiencing suicidal thoughts.

She and her family didn't know where to turn. Jane almost gave up. But then she heard about Dr. Leanne Williams' transformative new precision biotyping technology at Stanford.

Dr. Williams' team offered Jane the precision biotyping assessments and diagnosed a form of depression characterized by a blunting of the brain's reward circuit. This biotype is accompanied by anhedonia - loss of interest and motivation - and is unlikely to respond to traditional treatments.

After using a biotype-matched novel treatment targeting the anhedonia biotype Jane remitted in just 8 weeks.



The time is now. Every year, millions of people experience depression, anxiety, and other mental health conditions. The current diagnosis and treatment process is one of 'guess and check' relying on observed symptoms. It is insufficient to guide people to the right treatment sooner than is currently the case. On average time it takes 11 years for people to find treatment. Life can become overwhelmingly frustrating and, for all too many, life-threatening.

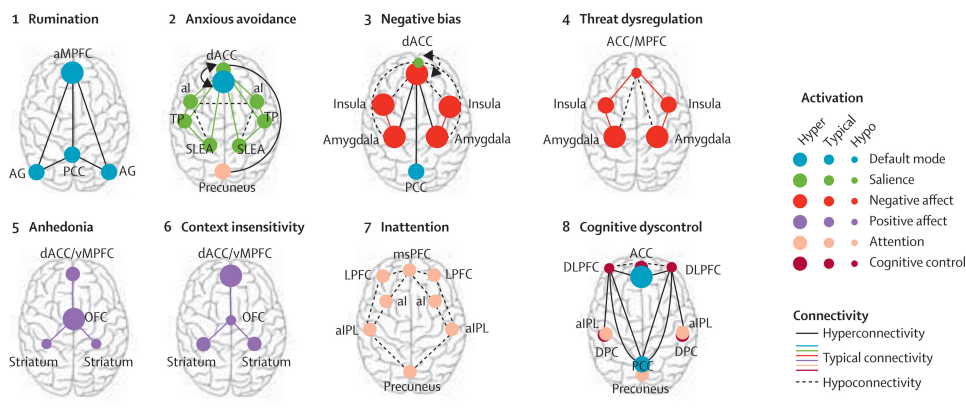
People's lives are at stake. Globally, one in five people experience a mood or anxiety disorder. These disorders affect young people in their most productive years, and can have a chronic impact across the entire lifespan. An estimated 75% of mental health disorders begin by 24 years of age, 50% by 14. Suicide claims a life every 40 seconds as reported by the World Health Organization. In the United States alone, annual costs related to depression related-illnesses, and lost workplace productivity exceed \$210 billion.

Personalized approaches are needed. Illnesses such as clinical depression are incredibly heterogeneous. Two people can be diagnosed with depression but only share one symptom. Despite this heterogeneity the current 'guess and check' approach considers everyone to be the same. There are no tests available to personalize diagnoses. Treatments are selected as 'one-size-fits-all'. Modern research has shown that the "typical patient" requiring 'one size' treatments does not exist, reflecting the need for more personalized approaches.

Taking up the challenge of personalized neuroscience. Clinical neuroscientist Dr. Leanne Williams believes that we need to reconceptualize mental health as brain health. She has spent more than 20 years focused on making this vision a reality. With the advent of brain imaging techniques with sufficient resolution to quantify neural connections in vivo, now is the time to reformulate mental disorders as neural circuit disorders. Dr. Williams has leveraged these rapid advances in brain imaging. She has focused on six major brain circuits that underlie cognitive, emotional, and self-reflective functions, the very functions that define human experience. Her work has documented how dysfunctions within and between these circuits gives rise to the symptoms that characterize different types of depression, anxiety and stress disorders. Dr. Williams' approach also offers a unique means to quantify the brain basis of the continuum of mental health through mental wellness.

Personalized Biotypes for tailoring interventions. Dr. Williams and her team have mapped the brain circuitry of thousands of individuals. The data sets have been acquired with a uniquely standardized approach to imaging so that data can be pooled. The samples include healthy people and people with multiple diagnoses, across ages 6 through 13 years. She has developed the world's first technology to diagnose specific biotypes based on these brain circuit measures. Her work identifies 8 biotypes that reflect different combinations of the six major circuits. Each biotype gives rise to specific symptoms, behaviors and risk factors.

Treatment outcomes using personalized biotyping are astonishing. Using her personalized biotype technology each person can be matched to the treatment that relieves the root cause of their symptoms. Dr. Williams' technology is the 'Rosetta stone' that translates an individual's mental health symptoms into the molecular treatment targets they need. Personalized biotyping identifies which specific compounds alleviate which specific types of human suffering. It informs which compounds to study and who may benefit from them and the magnitude of the benefit. Through personalized biotyping, Dr. Williams is able to guide the choice of treatment for depression, with a 71–81% cross-validated success rate in their initial clinical trials. This same personalized framework is now being used with emerging novel and exploratory therapeutics. It can be rapidly expanded to additional treatments and disorders.



Momentum is essential. To keep the momentum going, Dr. Williams launched the Center for Precision Mental Health and Wellness (PMHW), and serves as its director. She has partnered with Dr. Ruth O'Hara as Center Co-Director. Drs. Williams and O'Hara are the 'connectors' for multiple other faculty across the campus.

The Stanford Center for PMWH is poised to become the flagship center for a Moonshot for Brain Health given its location in Silicon Valley and the breadth and depth of multi-disciplinary collaborations across campus. The affiliate team is composed of specialties spanning neuroscience, psychology, genetics, engineering, computer sciences, global health, and AI and biomedical data sciences, all joining forces to bend the curve for mental health and to promote healthy lives for all.

We can bring hope across the world. Individuals and families want a solution for the mental health crisis. Personalized biotyping is that solution. To realize the full potential of personalized biotyping, acceleration is critical. Donor funding will ensure we accelerate beyond the serial approach of traditional funding mechanisms. By fast-tracking large longitudinal cohort trials biotyping will then be disseminated to other medical centers, enabling countless people around the world to benefit from this new technology developed here at Stanford. Additionally, the personalized biotyping platform can be expanded to other areas and therapies, and connected with digital approaches, at Stanford and beyond its walls.

THE CRISIS IN NUMBERS

#1

Depression is the main cause of disability globally.

20%

of Americans experience a mental illness,

70%

of people who seek care receive little benefit. .

\$1 Trillion

is the annual loss to the global economy..

Mr. A, aged 42, had experienced recurring depression all his life.

He was in fear of losing his job and had unsuccessfully tried 5 medications and was currently on 3 at once. A colleague referred him to our discovery clinic. We diagnosed a biotype characterized by cognitive impairment. This biotype does poorly on typical antidepressants and is associated with heightened risk of suicide and more work days lost.

After treatment with a biotype-matched novel treatment Mr. A remitted in 6 weeks. He has been motivated to return to work and start planning for the future!



OPPORTUNITIES FOR PARTNERSHIP

Create impact and advance precision mental health informed by neuroscience. With your partnership, we will fundamentally transform the care and understanding of mental illness and help millions of people live happier, more fulfilling lives.

Pilot Studies of Personalized Biotyping, targeting Novel Therapies
\$250,000 estimated per study

Larger Trials of Personalized Biotyping for Therapy vs Usual care.
\$1.2 million estimated per trial

Fully Funded Five-Year Acceleration of Personalized Biotyping in Longitudinal Cohort studies across the Lifespan.
\$7–\$8 million estimated

Flagship Precision Mental Health and Wellness Center Pooled Fund
Gifts of any size

PRINCIPAL INVESTIGATORS



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